

Amendments the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-45. (canceled)

46. (original) A pharmaceutical composition comprising CyaA or derivative or mutant or fragment or variant or peptide thereof.

47. (currently amended) A The pharmaceutical composition of claim 46, wherein said pharmaceutical composition is effective comprising CyaA or derivative or mutant or fragment or variant or peptide thereof as an adjuvant for immunization with a self or foreign antigen.

48. (currently amended) A The pharmaceutical composition of claim 46, further comprising CyaA or derivative or mutant or fragment or variant or peptide thereof in combination with an antigen, where wherein said antigen is selected from a self-antigen and a foreign antigen.

49. (currently amended) A The pharmaceutical composition as claimed in claims of claim 46 to 48 wherein the CyaA comprises a derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

50. (currently amended) A The pharmaceutical composition as claimed in of claim 46 to 49 wherein the self antigen is selected from any one or more of glutarnic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

51. (currently amended) A The pharmaceutical composition as claimed in of claim 50 wherein the antigens involved in graft rejection include antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney for graft recipient and neural graft components.

52. (currently amended) ~~A~~ The pharmaceutical composition ~~as claimed in any of claims claim 46 to 51~~ wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

53. (currently amended) ~~A~~ The pharmaceutical composition ~~as claimed in of claim 52~~ wherein the myelin protein is selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein (MOG) synthetic peptide, MOG peptide (35-55), and or peptides, fragments, mutants, and variants thereof.

54-55. (canceled)

56. (original) A pharmaceutical composition comprising non-acylated CyaA or derivative or mutant or fragment or variant or peptide thereof.

57. (original) An immunomodulator comprising adenylate cyclase toxin (CyaA).

58. (original) A recombinant non-acylated CyaA having immunomodulatory effects.

59. (original) A vaccine comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

60. (currently amended) ~~A~~ The vaccine ~~as claimed in of claim 59, further~~ comprising CyaA ~~or derivative or mutant or fragment or variant or peptide thereof and an antigen.~~

61. (currently amended) ~~A~~ The vaccine ~~as claimed in of claim 60~~ wherein the CyaA and antigen are present in a ~~by weight~~ ratio range of about 0.0 1: 1 to about 100: 1 by weight.

62. (currently amended) ~~A~~ The vaccine ~~as claimed in of claim 60~~ wherein the CyaA and antigen are present in a molar ratio of about 1: 10 to about 10:1.

63. (original) Antibodies to adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

64. (currently amended) ~~An~~ A peptide comprising an amino acid sequence selected from ~~any one or more of SEQ ID No. SEQ ID NO: 3 or SEQ ID NO: 4.~~

65. (currently amended) A method for the treatment and/or prophylaxis of a disorder selected from the group of disorders consisting of an inflammatory disorder and/or an immune-mediated disorder, comprising the step of administering an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

66. (canceled)

67. (currently amended) A ~~The method for the treatment and/or prophylaxis of~~ of claim 65, wherein the immune-mediated disorder is an autoimmune disease comprising the step of administering an agent comprising adenylate cyclase toxin (CyaA) or derivative or mutant or fragment or variant or peptide thereof.

68. (currently amended) A ~~The method as claimed in claims~~ of claim 65 to 67 wherein the agent comprises adenylate CyaA or derivative or mutant or fragment or variant or peptide thereof or a product of cells activated by these materials.

69. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 68 wherein the adenylate cyclase toxin (CyaA) is combined with self or foreign antigens or fragments or mutants or variants or peptides thereof.

70. (currently amended) A ~~The method as claimed in~~ of claim 69 wherein the self antigen is selected from any one or more of glutamic acid decarboxylase 65 (GAD 65), native DNA, myelin basic protein, myelin proteolipid protein, acetylcholine receptor components, thyroglobulin, thyroid stimulating hormone (TSH) receptor, Japanese cedar pollen antigens, ragweed pollen antigens, rye grass pollen antigens, and dust mite antigens and feline antigens for animal, histocompatibility antigens, antigens involved in graft rejection and an altered peptide ligand.

71. (currently amended) A ~~The method as claimed in~~ of claim 70 wherein the antigens involved in graft rejection comprise antigenic components of the graft to be transplanted into the heart, lung, liver, pancreas, kidney of graft recipient and neural graft components

72. (currently amended) A ~~The method as claimed in any of claims claim 69 to 71~~ wherein the self antigen is selected from any one or more of a myelin protein, beta amyloid protein, amyloid precursor protein and collagen and peptides thereof.

73. (currently amended) A ~~The method as claimed in~~ of claim 72 wherein the myelin protein is selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein (MOG) synthetic peptide, MOG peptide (35-55), and or peptides, fragments, mutants, and variants thereof.

74-75. (canceled)

76. (currently amended) A ~~The method as claimed in any of claims claim 65 to 75~~ wherein the adenylate cyclase toxin (CyaA) is derived from *Bordetella pertussis*, *Bordetella bronchiseptica* or *Bordetella parapertussis* or related molecules from other bacteria.

77. (currently amended) A ~~The method as claimed in any of claims claim 65 to 76~~ wherein the agent modulates inflammatory cytokine production.

78. (currently amended) A ~~The method as claimed in any of claims claim 65 to 77~~ wherein the immunomodulatory effects of CyaA on cells of the innate immune system is dependent on co-activation with a Toll-like receptor ligand.

79. (currently amended) A ~~The method as claimed in~~ of claim 78 wherein the Toll-like receptor ligand is LPS or another toll-like receptor ligand, selected from any one or more of CpG motifs, dsRNA, Poly (I:C) and the lipopeptide Pam3Cys.

80. (currently amended) A ~~The method as claimed in any of claims claim 65 to 79~~ wherein CyaA has an activity selected from the group of activities consisting of: promotes IL 10 and IL-6 production by macrophages and dendritic cells; synergises with LPS to promote IL-10 and IL-6 production by macrophages and dendritic cells; inhibits inflammatory cytokines, chemokines or other inflammatory mediators; promotes dendritic cell maturation following co-activation with TLR-ligands; promotes CD80 expression by dendritic cells; inhibits TLR ligand-induced dendritic cell activation; inhibits CD40 and ICAM-1 expression; acts as an adjuvant *in vivo* to

promote the induction of Th2 or Tr cells to co-administered antigens; and, acts as an adjuvant *in vivo* to promote IgG1 antibodies to co-administered antigens.

81-82. (canceled)

83. (currently amended) A ~~The method as claimed in~~ of claim 82 80 in which the CyaA inhibits inflammatory cytokines, and wherein the inflammatory cytokine is selected from any one or more of IL-12 or TNF- α , IFN- γ , IL-1, IL-23 and IL-27.

84. (currently amended) A ~~The method as claimed in~~ claim 82 80 in which the CyaA inhibits inflammatory chemokines, and wherein the inflammatory chemokine is macrophage inflammatory protein-1 α or macrophage inflammatory protein 1- β .

85-89. (canceled)

90. (currently amended) A ~~The method as claimed in~~ of claim 89 80 wherein the co-administered antigens comprise self or foreign antigens.

91-92. (canceled)

93. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 92 wherein the CyaA is present in a non-palmitoylated or non-acylated form.

94. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 93 wherein the CyaA is substantially endotoxin free.

95. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 94 wherein the CyaA is in the form of an immunomodulator, adjuvant, immunotherapeutic or antiinflammatory agent.

96. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 95 wherein the agent modulates inflammatory cytokine production induced by infection or trauma.

97. (currently amended) A ~~The method as claimed in any of claims~~ claim 65 to 96 wherein the disorder is a disorder selected from the group of disorders consisting of sepsis, or acute

inflammation induced by infection, acute inflammation induced by trauma, or acute inflammation induced by injury, Crohn's disease, inflammatory bowel disease, multiple sclerosis, type 1 diabetes, rheumatoid arthritis, psoriasis, asthma, and atopic disease.

98-99. (canceled)

100. (currently amended) A ~~The method as claimed in any of claims claim 65 to 99 in~~ wherein the agent is in a form for oral, intranasal, intravenous, intradermal, subcutaneous or intramuscular administration.

101. (currently amended) A ~~The method as claimed in any of claims claim 65 to 100~~ comprising repeated administration of the agent.

102. (new) The method claim 65 wherein the immune-mediated disorder is selected from the group consisting of diabetes mellitus, arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, osteoarthritis, psoriatic arthritis, myasthenia gravis, systemic lupus erythematosus, autoimmune thyroiditis, dermatitis, atopic dermatitis, eczematous dermatitis, Sjogren's Syndrome, keratoconjunctivitis sicca secondary to Sjogren's Syndrome, alopecia areata, allergic responses due to arthropod bite reactions, aphthous ulcer, iritis, conjunctivitis, keratoconjunctivitis, ulcerative colitis, asthma, allergic asthma, cutaneous lupus erythematosus, scleroderma, vaginitis, proctitis, drug eruptions, leprosy reversal reactions, erythema nodosum leprosum, autoimmune uveitis, allergic encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, idiopathic bilateral progressive sensorineural hearing loss, aplastic anemia, pure red cell anemia, idiopathic thrombocytopenia, polychondritis, Wegener's granulomatosis, chronic active hepatitis, Stevens-Johnson syndrome, idiopathic sprue, lichen planus, Graves ophthalmopathy, sarcoidosis, primary biliary cirrhosis, uveitis posterior, interstitial lung fibrosis, Alzheimer's disease and coeliac disease.